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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,352	01/30/2004	Barry J. Maurer	9022-41	4884

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
10/27/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/767,352	MAURER ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 August 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,13 and 15-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9,13 and 15-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/08/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt extension of time, declaration under 37 CFR 1.132, request for continued examination under 37 CFR 1.114, amendment and remarks, all filed 18/13/09. The examiner also acknowledges receipt of IDS filed 10.08.09. Claims 3 and 15 are amended. New claim 23 is added. Claims 2-9, 13 and 15-23 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/13/09 has been entered.

2.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 15-22, 2-9 and 13 remain provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 14-21 and 25 and 1-12 of copending Application Nos. 11/170,561 for reasons of record and reiterated herein below.

5. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims are directed to the same method of treatment using retinide. Retinide encompasses the specific retinide recited in claim 2.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

6. Applicant has indicated that a Terminal Disclaimer would be provided upon the indication of allowable subject matter. However, the provisional obviousness type double patenting rejection is not the only rejection in the examined application and the rejection will continue to be made until the rejection is overcome as stated in MPEP 804 [R-5], I B, that "the "provisional" double patenting rejection should continue to be made by the examiner in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in at least one of the applications." As noted above, the provisional obviousness double patenting rejection is not the only rejection remaining in this examined application. Thus rejection is maintained and is not held in abeyance.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 2-9, 13 and 15-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maurer et al. (US 6,352,844) in view of Yesair (US, 4874,795, Yesair I) or Yesair (US 5,972,911) and further in view of Gibbs et al. (US 4,665,098) and Weith (US 4,327,116).

10. Maurer teaches method of treating hyperproliferative disorder to a subject in need thereof (abstract; column 1, lines 35-46); the method comprises administering composition comprising fenretinide (column 7, line 35 to column 8, line 67); for oral administration, powders are suspended or made into solution in the presence of carriers (column 14, lines 12-67) such as sucrose, tragacanth and glycerin (column 15, lines 1-4). Treating hyperproliferative disorder meets the method of claim 15 and some examples of the disorder named are "tumors, **cancers,**

and neoplastic tissue that can be treated by the present invention include but are not limited to malignant disorders such as breast **cancers**; osteosarcomas; angiosarcomas; fibrosarcomas and other sarcomas; leukemias; lymphomas; sinus tumors; ovarian, uretal, bladder, prostate and other genitourinary **cancers**; colon esophageal and stomach **cancers** and other gastrointestinal **cancers**; lung **cancers**; myelomas; pancreatic **cancers**; liver **cancers**; kidney **cancers**; endocrine **cancers**; skin **cancers**; and brain or central and peripheral nervous (CNS) system tumors, malignant or benign, including gliomas and neuroblastomas;" and "examples of premalignant and non-neoplastic or non-malignant **hyperproliferative disorders** include but are not limited to myelodysplastic disorders; cervical carcinoma-in-situ; familial intestinal polyposes such as Gardner syndrome; oral leukoplakias; histiocytoses; keloids; hemangiomas; hyperproliferative arterial stenosis, inflammatory arthritis; hyperkeratoses and papulosquamous eruptions including arthritis. Also included are viral induced hyperproliferative diseases such as warts and EBV induced disease (i.e., infectious mononucleosis), scar formation, and the like" (column 5, lines 42-66). Maurer states that the methods of treatment may be employed with any subject known or suspected of carrying or at risk of developing a **hyperproliferative disorder** (column 5, lines 66 and 67). Fenretinide meets claims 15, 2 and claim 23 because for claim 23, the retinide of Maurer is capable of generating ceramide.

11. Maurer does not teach the carriers recited in the claims. However, Yesair I and II disclose oral delivery of fenretinide in a composition that comprises the fenretinide, lysophosphatidyl choline, fatty acid and monoglycerides (abstract; column 4, lines 35-65; column 5, lines 60-67; Example III). Also, Gibbs teaches fenretinide composition that comprises fenretinide or retinide, corn oil, non-ionic surfactant and that the composition can be

delivered by mixing in food, spread on bread or crackers or by filing the composition in a soft or hard gelatin capsule, and can also be delivered in powdered form (column 3, lines 3-7, column 1, lines 60-65). Thus the teaching of delivery by way of food meets claims 16 and 17 and further renders obvious claim 11. The fat and monoglycerides and lysophosphatidyl choline meet the requirements of claims 15, 3. Regarding claims 19 and 20, the geriatric and pediatric subjects read on Maurer's suggestion that the methods of treatment may be employed with any subject known or suspected of carrying or at risk of developing a **hyperproliferative disorder** (column 5, lines 66 and 67). The mode of feeding recited in claims 21 and 22 are known methods of feeding a subject needing this mode of feeding. Weith teaches that flour is a thickening agent. Claim 15 is amended to say that the flowable powder comprises retinide and the excipients recited. But, Gibbs teaches fenretinide composition that comprises fenretinide or retinide, corn oil, non-ionic surfactant and that the composition can be delivered by mixing in food, spread on bread or crackers or by filing the composition in a soft or hard gelatin capsule, and can also be delivered in powdered form (column 3, lines 3-7, column 1, lines 60-65). Thus, the composition of Maurer in combination with Yesair I or Yesair II and Gibbs in the form of a powder would also contain all the components of the composition including the excipients as according to the composition Maurer in view of Yesair.

12. Therefore, taking the teaching of the prior art, one having ordinary skill in the art at the time the invention was made would have reasonable expectation of success that modifying the composition of Maurer by using the carrier of Yesair I or II, and delivering the formulation as food item as suggested by Gibbs, the food item having been thickened by flour, would be easily administered to any patient including geriatric or pediatric patient.

Response to Arguments

13. Applicant's arguments filed 8/13/09 have been fully considered but they are not persuasive.

14. Applicant argues that the matrix of Yesair is a bitter tasting solid that rendered difficult compliance at clinical trial. But Yesair was relied upon to show that fenretinide is known to be formulated with lysophosphatidyl choline, fatty acid and monoglycerides. Lysophosphatidyl choline, fatty acid and monoglycerides are the excipients in claim 15 (b). The composition of Maurer comprises sucrose, a sweetener for the desired goal of administering to geriatric or pediatric patients, the sucrose would be expected to be employed in quantities that would render the preparation palatable to the geriatric and pediatric patient populations.

15. Applicant argues that Gibbs composition is a capsule, but, it is important that Gibbs clearly teaches that formulation containing fenretinde can be delivered in powder form in addition to the capsule form referred to by applicant.

16. Applicant is of the view that amending claim 15 to say that the dry flowable powder contains (a)-(d) overcomes the art, but because fenretinide has been contemplated to be delivered as a powder, then the composition of Maurer in view of Yesair I or II in powder form aloe contains the excipients disclosed by the combined references.

17. The declaration under 37 CFR 1./132 will be addressed below.

18. It is further noted that the rejection was made over combination of references and not made over Yesair I or II alone. Gibbs was relied upon for teaching that composition containing fenretinide is delivered in powdered form (column 3, lines 3-7, column 1, and lines 60-65) and is also noted that HPR is a fenretinide. Thus while Yesair I and II are directed to lipid colloid

composition, Gibbs discloses that powder formulation of fenretinide is also known to be administered so that fenretinide can be administered as a suspension or powder form. While Weith is directed to bakery products, Weith teaches that flour is a thickening agent. Therefore, applicant cannot show nonobviousness by attacking the references individually when the rejection is based on combination of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Declaration under 37 CFR 1.132 by Barry J. Maurer, MD, PHD:

19. The declaration under 37 CFR 1.132 filed 8/13/09 is insufficient to overcome the rejection of claims 2-9, 13 and 15-22 based upon rejections under 35 USC 103(a) over Maurer et al. (US 6,352,844) in view of Yesair (US, 4874,795, Yesair I) or Yesair (US 5,972,911) and further in view of Gibbs et al. (US 4,665,098) and Weith (US 4,327,116) as set forth in the last Office action because: Yesair was relied upon for formulating retinide with lysophosphatidyl choline, fatty acid and monoglycerides and not for the bitter tasting nature of it formulation.

20. The declaration centers its objection to Gibbs on the capsular form, but Gibbs suggest that retinide can be delivered as a powder and Gibbs is relied in the rejection for showing that fenretinide can be delivered as a powder and not that the composition is a capsule.

21. The declaration also states that fenretinide/LXS oral powder in mice produced much higher plasma levels and tissue levels than the Gibbs formulation at equivalent doses; that the sugar-flour composition produced higher levels in plasma and the brain than the LXS. But, there is no corresponding data to support the findings. Furthermore, claim 15 is directed to

composition that has components of the compositions recited in ranges and points outside the recited ranges and points within the recited ranges would be necessary for such a showing.

22. The declaration has referred to Appendix 8, which is data obtained form Phase I clinical trials of dose tolerance studies. But the study uses doses of fenretinide in $mg/m^2/day$ while the claims are not directed to mg doses per area per day. Thus, the clinical trial directed to doses of retinide does not provide any unexpected findings over the claims since the claims and the composition tested are not the same.

23. The declaration concludes by saying that the instant formulation is a new formulation for the delivery of fenretinide. But the formulation as recited is rendered obvious by the teachings of the combined reference. The composition tested is not the claimed composition.

24. No claim is allowed.

25.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Examiner, Art Unit 1618